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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/576,944	05/22/2000	Terry B. Strom	1440.1024-001	2729

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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	9

DATE MAILED: 07/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/576944	Applicant(s) STROM
	Examiner GAMBEL	Art Unit 1644

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☑ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 1-27

4a) Of the above claim(s) _____ is/are withdrawn from consideration. 1-10, 15-21

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 11-14, 22-27

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☑ The drawing(s) filed on 5/24/00 is/are: a)☐ accepted or b)☑ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

PAPER NO. -9-

DETAILED ACTION

1. Applicant's amendment, filed 3/29/02 (Paper No. 8), has been entered.
Claims 11, 13 and 14 have been amended.
Claims 22-27 have been added.

Claims 11-14 and 22-27 are being acted upon as the elected invention.

Again, applicant's election of Group II (claims 11-14) and the species B (anti-CD40L antibodies) in Paper No. 5 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

With respect to applicant traversal on the species of anti-CD40 antibodies, anti-CD40L antibodies, CD40-Ig and CD40L-Ig that no serious burden is placed on the examiner; MPEP 803 states that the Inventions be either independent or distinct and a burden on the Examiner if restriction is required. For the reasons of record, the structures of these costimulation blockade agents are distinct.
The requirement is still deemed proper and is therefore made FINAL.

Claims 1-10 and 15-21 stand withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention and species.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 3/29/02 (Paper No. 8)
The rejections of record can be found in the previous Office Action (Paper No. 5).

3. Formal drawings, filed 5/18/98, comply with 37 CFR 1.84.
Please see the form PTO-948 previously sent in Paper No. 6.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES
A. Correction of Informalities -- 37 CFR 1.85
New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, MUST be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings MUST be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in ABANDONMENT of the application.

4. The following is a quotation of the first paragraph of 35 U.S.C. § 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Upon reconsideration of applicant's amended claims, filed 3/29/02 (Paper No. 8), the previous rejection under 35 U.S.C. 112, first paragraph, scope of enablement, has been withdrawn.

6. Claims 26 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection

The specification does not provide adequate written description of the claimed invention, namely, "immunosuppressive agents", "apoptosis agents, "agonistic agents" and "antagonistic agents", as disclosed on pages 113-14 of the instant specification because the relevant identifying characteristics such as structure or other physical and/or chemical characteristics are not set forth in the specification as-filed.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Thus, the specification fails to describe these DNA sequences. The Court further elaborated that generic statements are not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function.

Finally, the Court indicated that while applicants are not required to disclose every species encompassed within a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, defined by nucleotide sequence, falling within the scope of the genus, See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicant is claiming a very broad generic class of molecules / agents, in the absence of the support of the disclosure of a limited representative number of species. The instant invention encompasses any agent encompassing immunosuppression and apoptosis as well as antagonists and agonists with no clear nature of said agonists/antagonists (e.g mechanisms of actions, endpoints, structure), yet the instant specification does not provide sufficient written description as to the critical structural features of said agents and the correlation between the chemical structure and the desired structural and/or function.

It has been well known that minor structural differences even among structurally related compounds or compositions can result in substantially different biological or pharmacological activities. Therefore, structurally unrelated agents encompassing immunosuppression, apoptosis, agonists and antagonists encompassed by the claimed invention would be expected to have greater differences in their structural and functional characteristics and attributes.

Mere idea or function is insufficient for written description; isolation and characterization at a minimum are required

Applicant is relying upon certain general and vague classes of agents to support entire genuses. The instant invention encompasses any "immunosuppressive agent", "apoptosis agent, "agonistic agent" and "antagonistic agent", yet the instant specification does not provide sufficient written description as to the structural features of said agents and the correlation between the chemical structure and the desired CD40 binding activity.

The instant claims do not provide functional characteristics coupled with a known or disclosed correlation between function and structure. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genuses, and because the genuses are highly variable, the instant disclosure is insufficient to describe the genuses of "immunosuppressive agents", "apoptosis agents, "agonistic agents" and "antagonistic agents", encompassed by the claimed fusion proteins.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

In the absence of structural characteristics that are shared by members of the genus of agents encompassed by the claimed invention, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genuses. Thus, Applicant was not in possession of the claimed genuses. See University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

"It is not sufficient to define the recombinant molecule by its principal biological activity, e.g. having protein A activity, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property." Colbert v. Lofdahl, 21 USPQ2d, 1068, 1071 (BPAI 1992).

Applicant has failed to provide sufficient written description for "immunosuppressive agents", "apoptosis agents, "agonistic agents" and "antagonistic agents, encompassed by the claimed invention.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

7. Upon reconsideration of applicant's amended claims, filed 3/29/02 (Paper No. 8), the previous rejection under 35 U.S.C. § 102(e) as being anticipated by de Boer et al. (U.S. Patent No. 5,869,050), has been withdrawn.

8. Upon reconsideration of applicant's amended claims, filed 3/29/02 (Paper No. 8), the previous rejection under 35 U.S.C. § 102(e) as being anticipated by de Boer et al. (U.S. Patent No. 5,747,034) has been withdrawn.

9. Upon reconsideration of applicant's amended claims, filed 3/29/02 (Paper No. 8), the previous rejection under 35 U.S.C. § 103(a) as being unpatentable over de Boer et al. (U.S. Patent No. 5,869,050) AND/OR de Boer et al. (U.S. Patent No. 5,747,034) in view of Kelly et al. (U.S. Patent No. 5,118,493) has been withdrawn.

10. Claims 11, 13, 14, 22 and 24-27 are rejected under 35 U.S.C. § 102(e) as being anticipated by Chen et al. (U.S. Patent No. 5,990,109). Chen et al. teach compositions comprising at least CD40L-specific antibodies and immunosuppressive agents comprising rapamycin (see entire document, including Detailed Description of the Invention, particularly column 21, paragraphs 1-3 and claims 37-38). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced antibodies and immunosuppressive agents. Although, the term "kit" is not specifically taught by the reference, there is no recitation that separates the prior art compositions comprising the same active ingredients as the instant claims.

Applicant's arguments, filed 3/29/02 (Paper No. 8), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant argues that Chen et al. do not disclose compositions comprising at least CD40L-specific antibodies and immunosuppressive agents. However, applicant acknowledges that Chen et al. does disclose heterocyclo-substituted imidazopyrazine compounds and compositions employed as protein tyrosine kinase inhibitors. Applicant also acknowledge that the compounds may be employed alone or in combination with each other as suitable therapeutic agents. Applicant acknowledges that the exemplary blocking agents include CD40:CD40L inhibitors. Applicant argues that Chen et al. does not disclose or claim composition of such agents which do not also include heterocyclo-substituted imidazopyrazine compounds and do not disclose kits.

However, Chen et al. does disclose compositions comprising Rapamycin (see column 21, paragraphs 1-3, including column 21, lines 37-38).

Further, it is noted that the claimed methods recite "comprising" which leaves the claim open for the inclusion of unspecified ingredients even in major amounts. See MPEP 2111.03.
Therefore, the claims can encompass heterocyclo-substituted imidazopyrazine compounds.

Again applicant has not distinguished the prior art teaching of compositions from the claimed recitation of "kit", wherein the prior art compositions comprising the same active ingredients as the instant claims.

. Applicant's arguments are not found persuasive

11. Claims 11, 13, 14, 22 and 24-27 are rejected under 35 U.S.C. § 102(e) as being anticipated by Nadler et al. (U.S. Patent No. 5,962,415). Nadler et al. teach compositions comprising at least CD40L-specific antibodies and immunosuppressive agents comprising rapamycin (see entire document, including Detailed Description of the Invention, particularly column 8, paragraphs 1-3). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced antibodies and immunosuppressive agents. Although, the term "kit" is not specifically taught by the reference, there is no recitation that separates the prior art compositions comprising the same active ingredients as the instant claims.

Applicant's arguments, filed 3/29/02 (Paper No. 8), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant argues that Nadler et al. does not disclose compositions comprising CD40L-specific antibodies, nor compositions comprising rapamycin.

However, Nadler et al. does teach that the inhibitors of gp39 (i.e. CD40L) can take the form of antibody component peptides (see column 8, lines 30-33 and 39).

However, Nadler et al. does teach immunosuppressant compositions comprising rapamycin (see column 7, paragraph lines 54-62).

Again applicant has not distinguished the prior art teaching of compositions from the claimed recitation of "kit", wherein the prior art compositions comprising the same active ingredients as the instant claims.

Applicant's arguments are not found persuasive

12. Claims 11-14 and 22-27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over de Noelle et al. (U.S. Patent No. 5,942,229) in view of Chen et al. (U.S. Patent No. 5,990,109) AND/OR Nadler et al. (U.S. Patent No. 5,962,415) and further in view of Kelly et al. (U.S. Patent No. 5,118,493) (1449).

Applicant's arguments, filed 3/29/02 (Paper No. 8), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal concerning the teachings of Chen et al. and Nadler et al. are essentially the same as set forth above.

Applicant arguments concerning the teachings of Chen et al. With respect to heterocyclo-substituted imidazopyrazine compounds and of Nadler et al. With respect to inhibitors of nuclear protein translocation that these inhibitors do not share the same properties of applicant's claimed costimulation blockade agents is acknowledged. In addition, applicant argues that Chen et al. And Nadler et al. Focus on agents that are not agents claimed by applicants.

However, these teachings are clear in that compositions comprising inhibitors, including immunosuppressive agents of diverse structures, biological and pharmacological activities can be combined, given the desired endpoints of inhibiting targeted responses of interests.

Clearly, the prior art taught that both rapamycin and CD40L-specific antibodies were useful as immunosuppressants, including the inhibition of graft rejection and that both rapamycin and CD40L-specific antibodies could be combined with other immunosuppressants to achieve the desired immunosuppression.

Again, Noelle et al. teach the coadministration of two immunosuppressive agents comprising CD40L-specific antibodies (see columns 10-11, Section V) as well as art known compositions (see columns 8-10, Section IV.)and immunosuppressants (see entire document).

Noelle et al. differs from the claimed invention by teaching art known immunosuppressant rapamycin per se and by not disclosing the use of fish oils as the type of oil suitable for the compositions or formulations taught for immunosuppression.

In contradistinction with Chen et al. and Nadler et al., Noelle et al. provides the expectation of success and motivation that CD40L-specific antibodies was a key ingredient of immunosuppressive formulations.

Kelly et al. teach the use of fish oils for immunosuppressive agents such as cyclosporin (see entire document).

Given the reduced nephrotoxicity associated with fish oils with immunosuppressive agents as taught by Kelly et al.; one of ordinary skill in the art at the time the invention was made would have been motivated to select such fish oils as a suitable oil for immunosuppressive compositions and formulations as taught by de Noelle et al., Chen et al. and Nadler et al. in immunosuppressive regimens.

While the claim recites a kit, no positive recitation of the ingredients distinguishes it over the references; therefore the kit is encompassed by the references. However, if this is not the case, it is a well known convention in the art to place these components in a kit for convenience and economy.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

13. No claim is allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Patent Examiner
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